

9. A purified polypeptide according to claim 1, said polypeptide comprising a portion of the human Asp2(b) amino acid sequence set forth in SEQ ID NO: 6 effective to cleave APP, said polypeptide lacking transmembrane domain amino acid residues 430-452 of SEQ ID NO: 6

10. A purified polypeptide according to claim 1, comprising the murine Asp2 amino acid sequence set forth in SEQ ID NO: 8, or a fragment thereof that cleaves APP.

11. A purified polypeptide according to claim 1 comprising a fragment of a mammalian Asp2 polypeptide, wherein the purified polypeptide lacks the transmembrane domain of said mammalian Asp2 polypeptide.

12. A fusion protein comprising a polypeptide according to any one of claims 1-10, and which further includes a heterologous tag amino acid sequence.

13. A polypeptide according to any one of claims 1-12, wherein the polypeptide cleaves human APP or human APP-Sw at the  $\beta$ -secretase recognition site.

14. A polypeptide according to any one of claims 1-3, 5-7, or 9-13, wherein the polypeptide lacks any mammalian Asp2 pro-peptide sequence.

15. A polypeptide according to claim 14, beginning with the N-terminal sequence ETDEEP.

16. A polypeptide according to any one of claims 1-3, 5-7, 9, or 11-15, selected from the group consisting of:

(a) a polypeptide comprising a portion of the amino acid sequence set forth in SEQ ID NO: 4 effective to cleave APP, wherein the polypeptide lacks amino acids 1-45 of SEQ ID NO: 4; and

(b) a polypeptide comprising a portion of the amino acid sequence set forth in SEQ ID NO: 6 effective to cleave APP, wherein the polypeptide lacks amino acids 1-45 of SEQ ID NO: 6.

17. A purified polynucleotide comprising a nucleotide sequence that encodes a polypeptide according to any one of claims 1 to 16.

18. A polynucleotide according to claim 17, selected from the group consisting of:
- (a) a polynucleotide comprising the nucleotide sequence set forth in SEQ ID NO: 3;
  - (b) a polynucleotide comprising the nucleotide sequence set forth in SEQ ID NO: 5;
  - (c) a polynucleotide comprising the nucleotide sequence set forth in SEQ ID NO: 7;
  - (d) a polynucleotide comprising a nucleotide sequence that is at least 95% identical to (a), (b), or (c), and that encodes a polypeptide that cleaves APP; and
  - (e) a fragment of (a), (b), (c), or (d) that encodes a polypeptide that cleaves APP.
19. A polynucleotide according to claim 17 comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 21, 23, 25, 27, 29, and 31.
20. A purified polynucleotide according to claim 17, selected from the group consisting of:
- (a) a purified polynucleotide that comprises a nucleotide sequence that encodes amino acids 22-501 of SEQ ID NO: 4 and lacks adjacent nucleotide sequence encoding amino acids 1-21 of SEQ ID NO: 4; and
  - (b) a purified polynucleotide that comprises a nucleotide sequence that encodes amino acids 22-476 of SEQ ID NO: 6 and lacks adjacent nucleotide sequence encoding amino acids 1-21 of SEQ ID NO: 6.
21. A purified polynucleotide according to claim 17, selected from the group consisting of:
- (a) a purified polynucleotide comprising a nucleotide sequence that encodes a portion of the human Asp2(a) amino acid sequence set forth in SEQ ID NO: 4 effective to cleave APP, and wherein the polynucleotide lacks adjacent nucleotide sequence encoding transmembrane domain amino acid residues 455-477 of SEQ ID NO: 4; and
  - (b) a purified polynucleotide comprising a nucleotide sequence that encodes a portion of the human Asp2(a) amino acid sequence set forth in SEQ ID NO: 6 effective to cleave APP, and wherein the polynucleotide lacks adjacent nucleotide sequence encoding transmembrane domain amino acid residues 430-452 of SEQ ID NO: 6.
22. A purified polynucleotide according to claim 21, said polynucleotide lacking nucleotide sequence encoding amino acids 454-501 of SEQ ID NO: 4.

23. A purified polynucleotide according to claim 17 comprising a fragment of a mammalian Asp2 polynucleotide, wherein the fragment lacks nucleotide sequence encoding the transmembrane domain of said mammalian Asp2 polypeptide.

24. A purified polynucleotide according to claim 17, wherein the polynucleotide lacks a nucleotide sequence encoding a mammalian Asp2 pro-peptide sequence.

25. A vector comprising a polynucleotide according to any one of claims 17-24.

26. A vector according to claim 25 that is an expression vector wherein the polynucleotide is operably linked to an expression control sequence.

27. A host cell transformed or transfected with a polynucleotide according to any one of claims 17-24.

28. A host cell transformed or transfected with a vector according to claim 25 or 26.

29. A host cell according to claim 28 that is a mammalian cell.

30. A host cell according to claim 28 or 29 that expresses the polypeptide on its surface.

31. A host cell according to claim 28 or 29 that secretes the polypeptide encoded by the polynucleotide, wherein the secreted polypeptide lacks a transmembrane domain.

32. A host cell according to any one of claims 27-31, wherein the host cell is transfected with a nucleic acid comprising a nucleotide sequence that encodes an amyloid precursor protein (APP) or fragment thereof that includes a protease recognition site recognized by the polypeptide.

33. A host cell according to claim 32, wherein the host cell is transfected with a nucleic acid comprising a nucleotide sequence that encodes an amyloid precursor protein (APP).

34. A host cell according to claim 33, wherein the host cell is transfected with a nucleic acid comprising a nucleotide sequence that encodes an amyloid precursor protein (APP) that includes two carboxy-terminal lysine residues.